

F.D.A. Review Criticizes Diabetes Drug and Maker

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Patients who take Avandia, a popular but controversial [diabetes](#) medicine made by GlaxoSmithKline, are far more likely to suffer and die from heart problems than those who take Actos, a similar pill made by Takeda, according to federal drug reviewers.

Avandia is particularly dangerous to patients who also take insulin. By contrast, Actos can be taken safely with insulin, according to the review.

The findings likely spell the end of Avandia's status as one of the nation's most popular drugs for treating diabetics who are not dependent on insulin. Last year, more than a million patients in the United States took Avandia, and a similar number took Actos.

Avandia's 2006 global sales were nearly \$3.4 billion.

The report and charges that GlaxoSmithKline sought to intimidate a doctor who publicly warned about Avandia's risks in 1999 could lead to a cascade of lawsuits against GlaxoSmithKline. Indeed, F.D.A. reviewers were sharply critical of the quality of the studies GlaxoSmithKline has undertaken to test the safety of Avandia, dismissing the present and future results of an ongoing 4,000-patient trial as unreliable and invalid.

The report by medical and safety reviewers within the [Food and Drug Administration](#) also provides ammunition to critics on Capitol Hill and elsewhere who claim that top F.D.A. officials have been far too slow to acknowledge Avandia's risks. GlaxoSmithKline suggested a year ago that the agency add a note to the drug's label about Avandia's growing heart risks, the report states.

At another point in the report, an F.D.A. safety reviewer, David Graham, concluded that a safety alert released by top F.D.A. officials on May 21 falsely reassured patients that at least one large Avandia study showed that the drug was safe.

That study, Dr. Graham concluded, provided no such reassurance.

These conclusions come in a 436-page compendium of reviews released in advance of an advisory committee hearing to be held on Monday to discuss Avandia's effects on the heart.

The F.D.A. intends to ask the committee of independent experts whether Avandia should continue to be sold. It is far from clear, F.D.A. safety reviewers concluded in the report, whether taking Avandia, also known as rosiglitazone, is worth the risk.

“A critical question to be resolved in determining appropriate regulatory action is whether the anticipated therapeutic benefit of rosiglitazone outweighs the demonstrated cardiovascular risk,” one F.D.A. reviewer concluded.

In 2000, the F.D.A. asked Warner-Lambert to remove Rezulin from the market because that drug caused more liver problems than either Actos or Avandia, both of which were approved for sale in 1999 and provided similar benefits.

Avandia's heart risks are likely to injure far more patients than Rezulin's rare but serious effects on the liver. Most diabetics die of [heart disease](#).